

AMENDMENTS TO THE SPECIFICATION

Please add the following new paragraphs after paragraph [0043] under the 'BRIEF DESCRIPTION OF DRAWINGS' section.

[0044] FIG. 16 is a graphical display showing the relative binding curves of 2D12.5 for Y-DOTA isomers and Y-DPTA. 2D12.5 binds both the (R)- and (S) isomers of 2-(4-nitrobenzyl)-DOTA when the coordinated metal is Y^{3+} (the same behavior is expected for the other rare earths). The (S)-isomer confers Λ -helicity, while the (R)-isomer with Δ -helicity, to the acetate arms. The Λ -helicity is observed in the crystal structure for 2D12.5 and is the preferred isomer for binding. However, the antibody tolerates the (R)-isomer with Δ -helicity, and the affinity decreases less than an order of magnitude as compared to the (S), Λ isomer. Y-DOTA (no-sidearm) exists in solution as a racemic mixture of the coordination isomers. As expected, the binding affinity for racemic Y-DOTA is between that observed for the (S)- and (R)-isomers of 2-(4-nitrobenzyl)-DOTA.

[0045] FIG. 17 is a graphical display showing the relative binding curves of Y-DOTA molecules with different sidechain locations. Changing the location of the sidechain of DOTA causes a decrease in the binding affinity, but the affinity of the (5-Amino-2-methoxy-phenyl)-carboxymethyl)-DOTA is still sufficiently strong to consider for further applications. Evaluation of the crystal structure seems to indicate that shorter substitutions at this position may bind with higher affinity. Substitutions at the other locations may yield reasonably high affinities as well. The (5-Amino-2-methoxy-phenyl)-carboxymethyl)-DOTA analyzed in this experiment was racemic, so it is not clear which isomer binds with higher affinity. The low pKa of the carboxymethyl proton makes it difficult to prepare a chirally pure molecule. Substitution as observed in the (S)-2-(4-nitrobenzyl)-DOTA is clearly stronger.